

# Management of Concomitant Risk & Co-Morbid Conditions in Hypertensive Pts

- Case Presentation #1: A closer look at concomitant risk & co-morbid conditions
- Objectives of Treatment
- Hyperlipidemia
- Impaired Fasting Glucose
- Diabetes

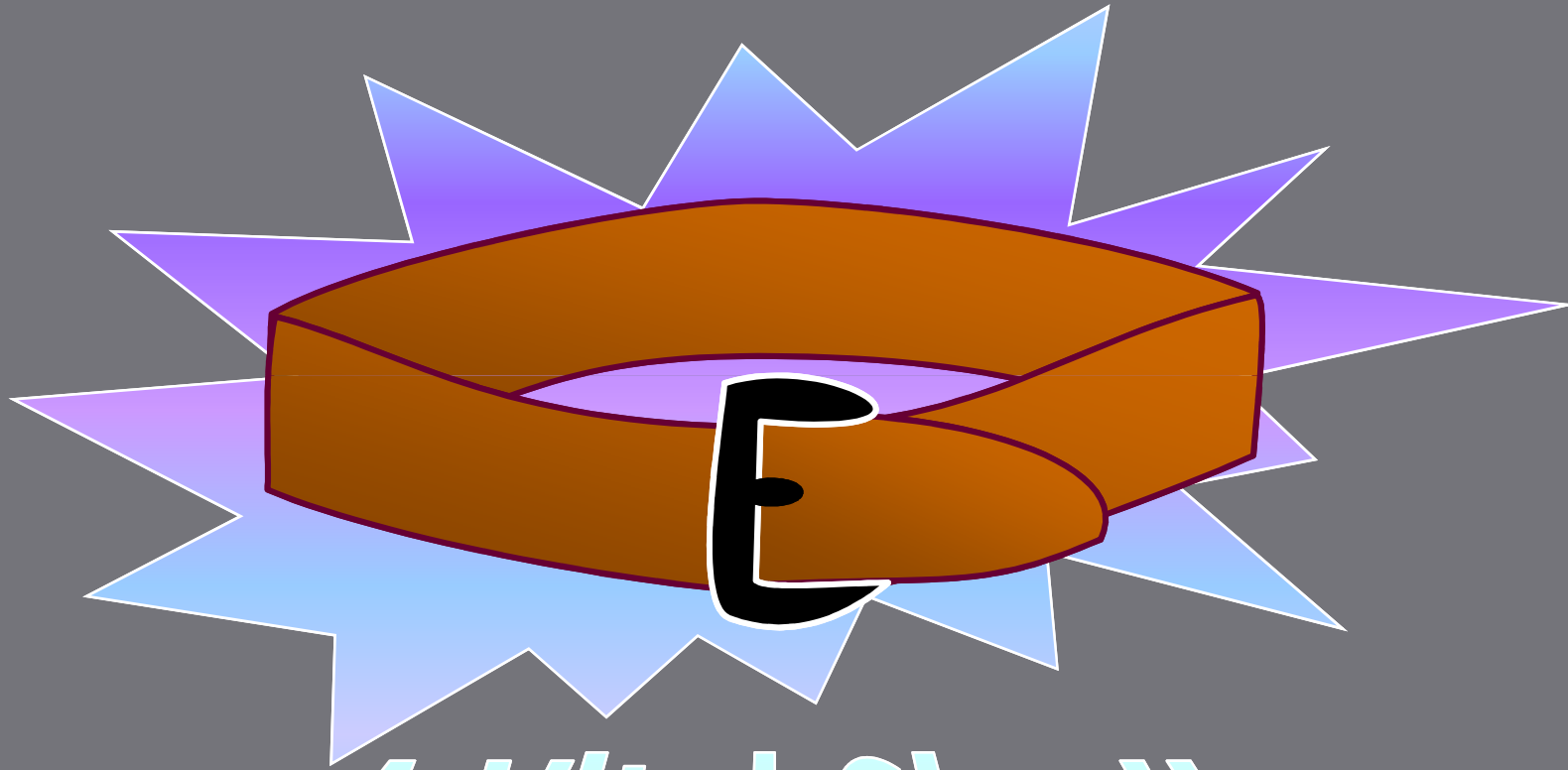
# Case Presentation #1: Elderly Hypertensive

- Hx. You are seeing Mrs. E. Jones for the 1<sup>st</sup> time. She is a 68 y/o AAF who cared for her husband during an extended terminal illness. She ran out of little 'blue pills' for HTN 6 months ago. She is asymptomatic and has no h/o CVD, CKD, diabetes, or ↑ cholesterol. *She has a strong FH of HTN, T2D, CVD and ESRD*
- Exam: WDWN AAF BMI 26.9 WC 35" BP 162/98 Gr 1 /2 KW; no bruits, lungs clear, no ES, no edema
- Plan: You decide to instruct the patient on home BP monitoring; recommend DASH Eating Plan, walking 20 min daily; order lab tests; RV 2 wk

# Case Presentation #1: Elderly Hypertensive


- RV 2 wks: Mrs. EJ is feeling well, likes DASH , and has been walking 30 minutes daily. Her home BP, taken twice daily, averages 152/88
- Exam: BMI unchanged WC 35" BP **156/92**
- Lab: K+ 4.3 **Creat 1.4 (eGR 48)** TC 208 TG 78 HDL 52 **LDL 140 alb/creat 32 ECG LVH (voltage)**
- Plan: Mrs. EJ agrees to continue DASH and her walking program. You provide further counseling and develop a management plan with her.

**Elevated Waist Circumference:**  
*A Key Feature in Patients with the  
Metabolic Syndrome*



*A Vital Sign!!*

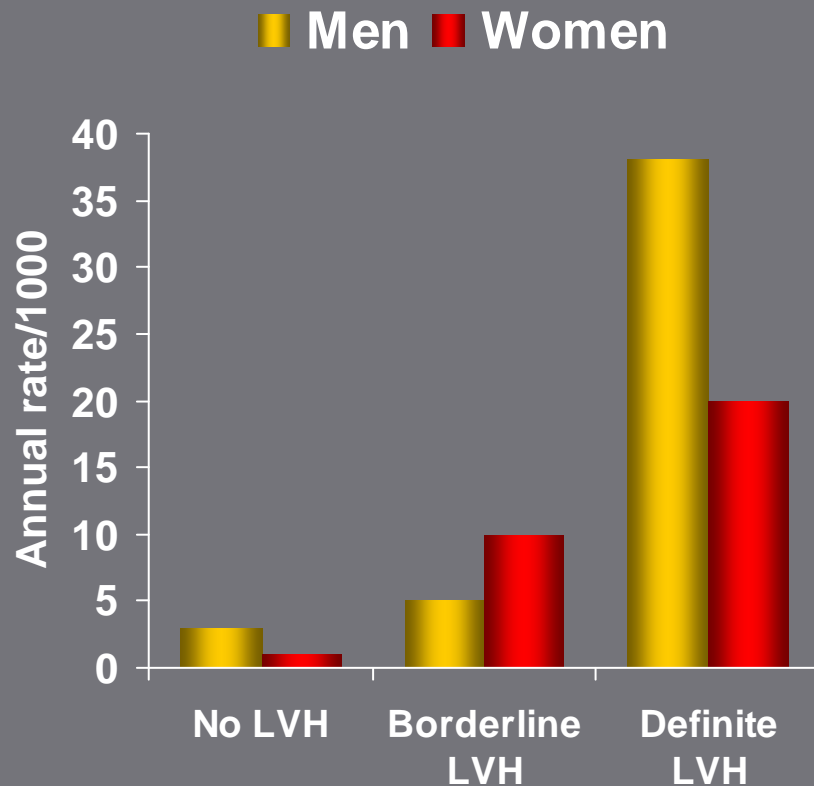
# Features of the Metabolic Syndrome Commonly Found among Viscerally Obese Patients

- 
- |                              |                           |
|------------------------------|---------------------------|
| • Hypertriglyceridemia       | • Insulin resistance      |
| • Low HDL cholesterol        | • Hyperinsulinemia        |
| • Elevated apolipoprotein B  | • Glucose intolerance     |
| • Small, dense LDL particles | • Impaired fibrinolysis   |
| • Inflammatory profile       | • Endothelial dysfunction |

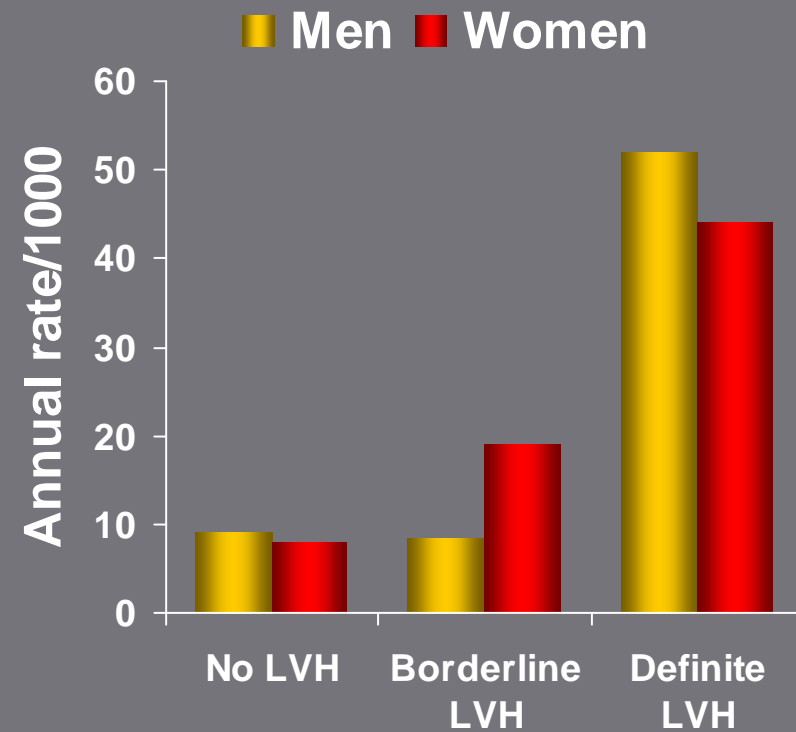
**Genetic susceptibility** to hypertension, type 2 diabetes, and coronary heart disease ultimately affects the clinical features of the metabolic syndrome.

# Incidence of CHF by LVH Status Stratified by Gender and Age

## The Framingham Heart Study



Age 35-64



Age 65-94

Cupples L, et al. *The Framingham Study*. NIH Publication No. 87-2703, 1987.

# Objectives & Goals of Therapy

## Objectives:

1. Prevent CV disease
2. Prevent progression to T2DM and nephropathy
3. Maintain and improve quality of life

## Goals of Treatment:

1. 5–10% wt loss (DASH), walk 30 minutes daily
2. BP <140/90 (<130/80) with regimen including ACEI or ARB
3. LDL-C <100 mg/dL (<70)
4. Regression of ECG - LVH (LIFE)
5. ? Reverse microalbuminuria

# Case Presentation #1: Elderly Hypertensive

- RV 8 weeks. Mrs. EJ continues to feel well, follow DASH & walk. Her home BP is 134/82. She is taking her benazepril 20/amlodipine 5 daily.
- Exam: BMI 26.5 BP 136/86 Lungs: clear  
Heart: RRR Ext: tr-1+ edema bilaterally
- Lab: K<sup>+</sup> 4.7 Creat 1.5 (eGFR 44) TC 202 HDL 54  
TG 64 LDL 135 alb/creat 18 mg/dL



# Case Presentation #1: Elderly Hypertensive

In addition to increasing her benazepril to 40 mg daily you decide to explain her LDL-goal, which is?

1. <190
2. <160
3. <130
4. <100
5. <70

# ATP III LDL-C Goals and Cutpoints for TLC and Drug Therapy in Different Risk Categories and Proposed Modifications Based on Recent Clinical Trial Evidence

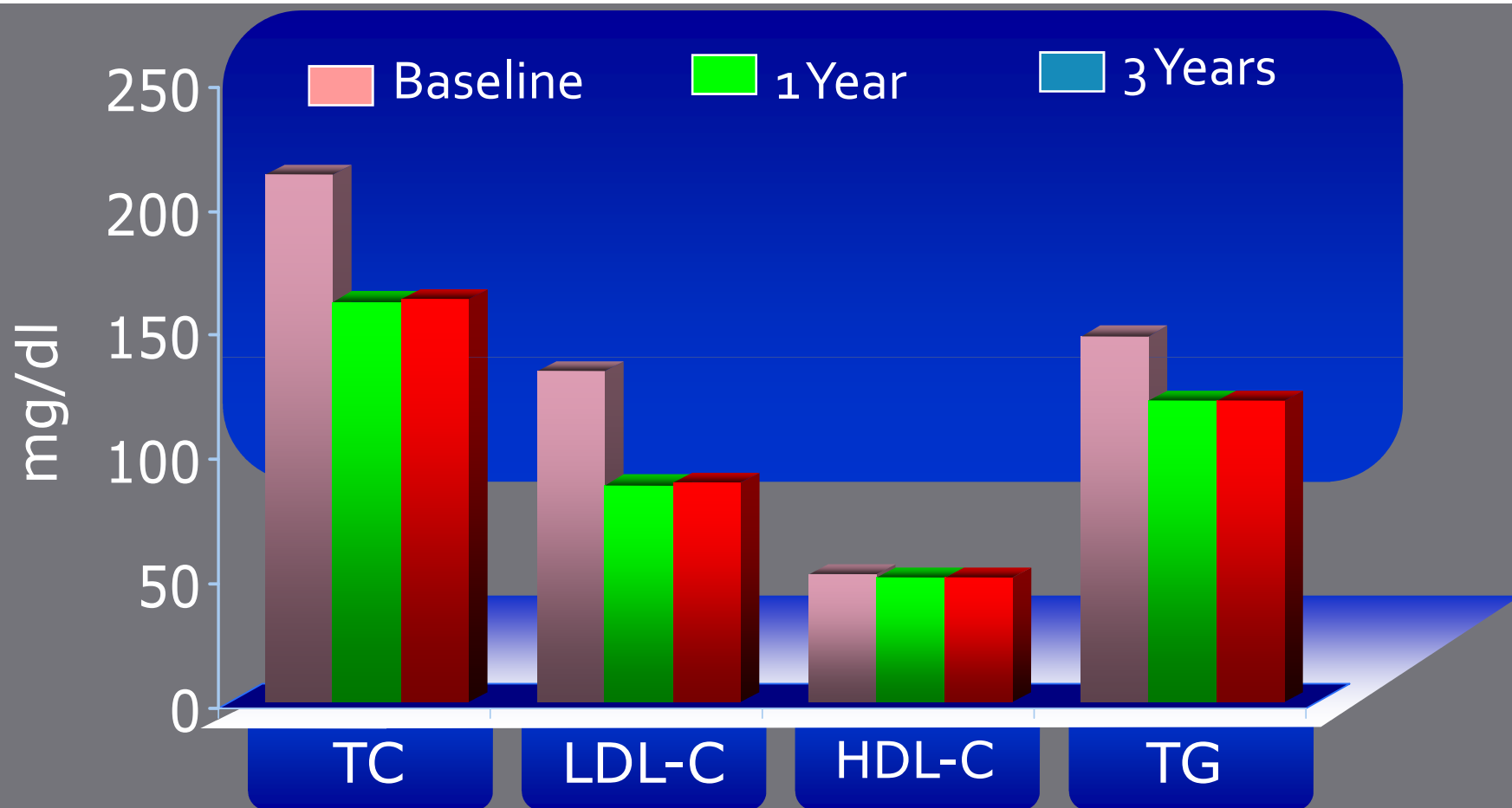
<u>Risk Category</u>	<u>LDL-C Goal</u>	<u>Initiate TLC</u>	<u>Consider Drug Rx**</u>
<i>High risk:</i>	<100 mg/dL optional < 70	$\geq 100$ >70	$\geq 100$ > 70 – 99
<i>Moderately high 2 risk factors‡ (10% to 20%)</i>	<130 optional <100	$\geq 130$ $\geq 100$	$\geq 130$ 100 - 129
<i>Moderate risk 2 risk factors‡ &lt;10%</i>	<130	$\geq 130$	$\geq 160$
<i>Lower risk: 0–1 risk factor &lt;10%</i>	<160	$\geq 160$	$\geq 190$

# Case Presentation #1: Elderly Hypertensive

Which of the following studies most directly supports treating Mrs. EJ with a statin?

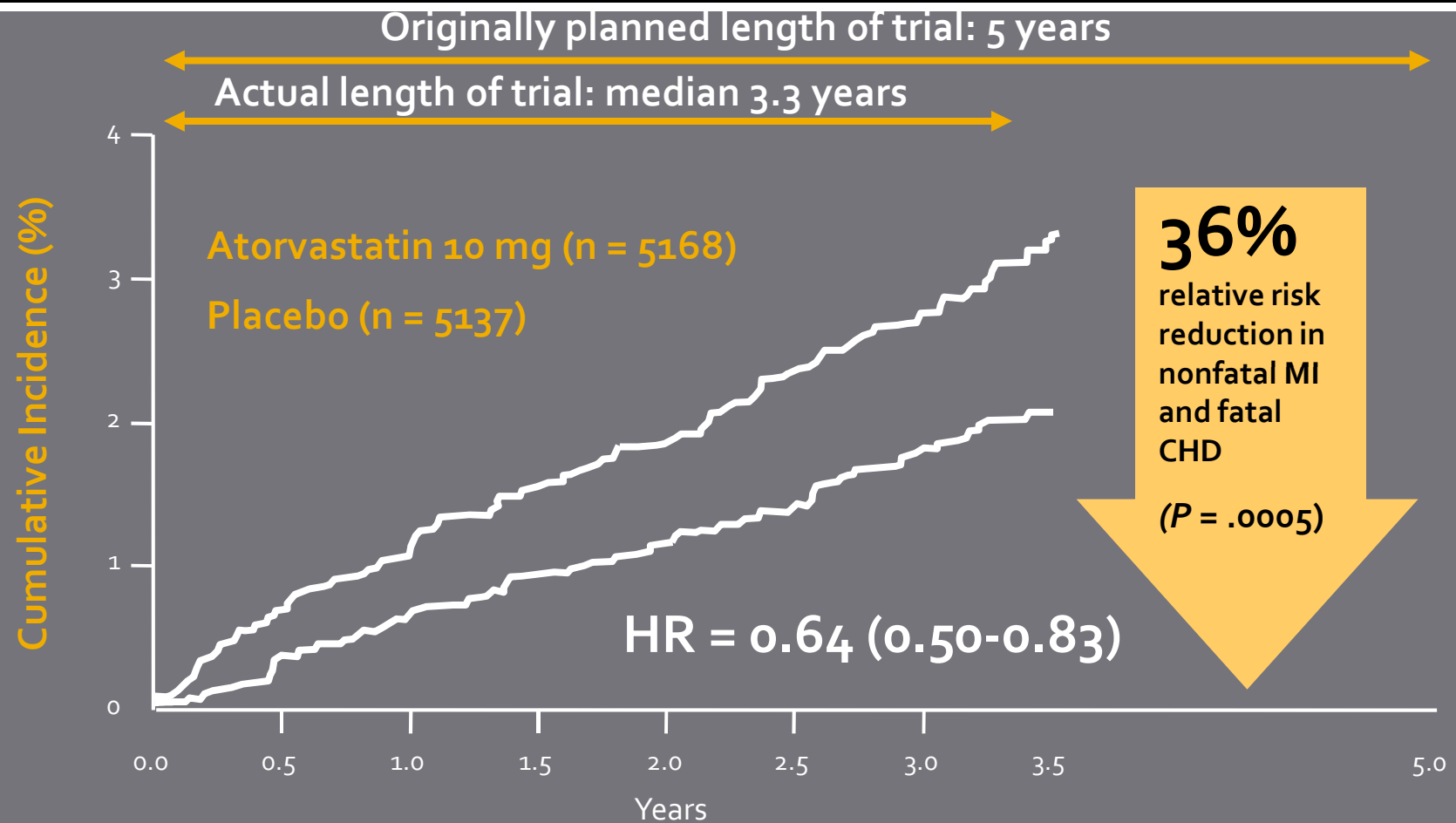
1. Heart Protection Study (HPS)
2. AFCAPs / TexCAPS
3. ASCOT – LLA
4. Scandinavian Simvastatin Survival Study (4s)
5. Treat to new target (TNT)

# ASCOT: Lipid Changes with Atorvastatin



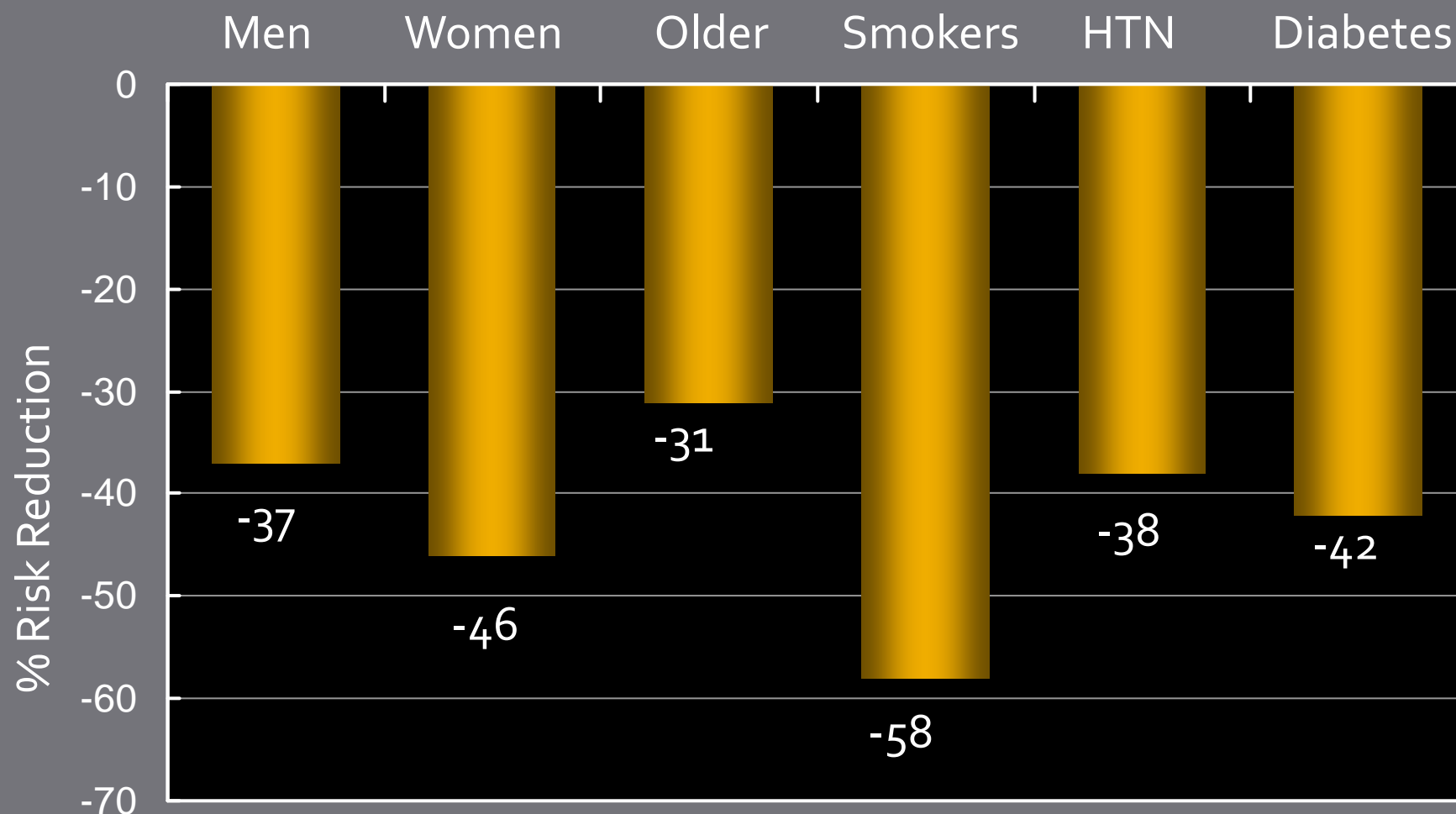
Sever PS et al. *Lancet* 2003;361:1149–1158.  
Reprinted with permission from Elsevier Science.

# ASCOT-LLA: Primary End Point— Nonfatal MI and Fatal CHD



Adapted from Sever PS, et al. *Lancet*. 2003;361:1149-1158.

# AFCAPS/TexCAPS: Subgroup Analysis



Lovastatin Reduced the Risk of Acute MCE

Downs JR et al. *JAMA* 1998;279:1615-1622.

# Case Presentation #1: Elderly Hypertensive

- RV 20 weeks. Mrs. EJ continues to feel well, but is not following her DASH & walking program as well. Her home BP is 130/78. She is taking her benazepril 40 / amlodipine 5 daily; simvastatin 20 mg daily.
- Exam: BMI 26.5 BP 132/82 Lungs: clear  
Heart: RRR Ext: tr bilaterally
- Lab: K<sup>+</sup> 4.8 Creat 1.5 (eGFR 44) TC 160 HDL 55  
TG 58 LDL 93 alb/creat 14 mg/dL FBS 104

# Modulation of Glomerular Capillary Filtration Pressure

Dilate afferent → ↑ GCP:  
Obesity, ↓ nephrons,  
dCCB, high protein,  
high Na<sup>+</sup>, high glucose

Afferent arteriole

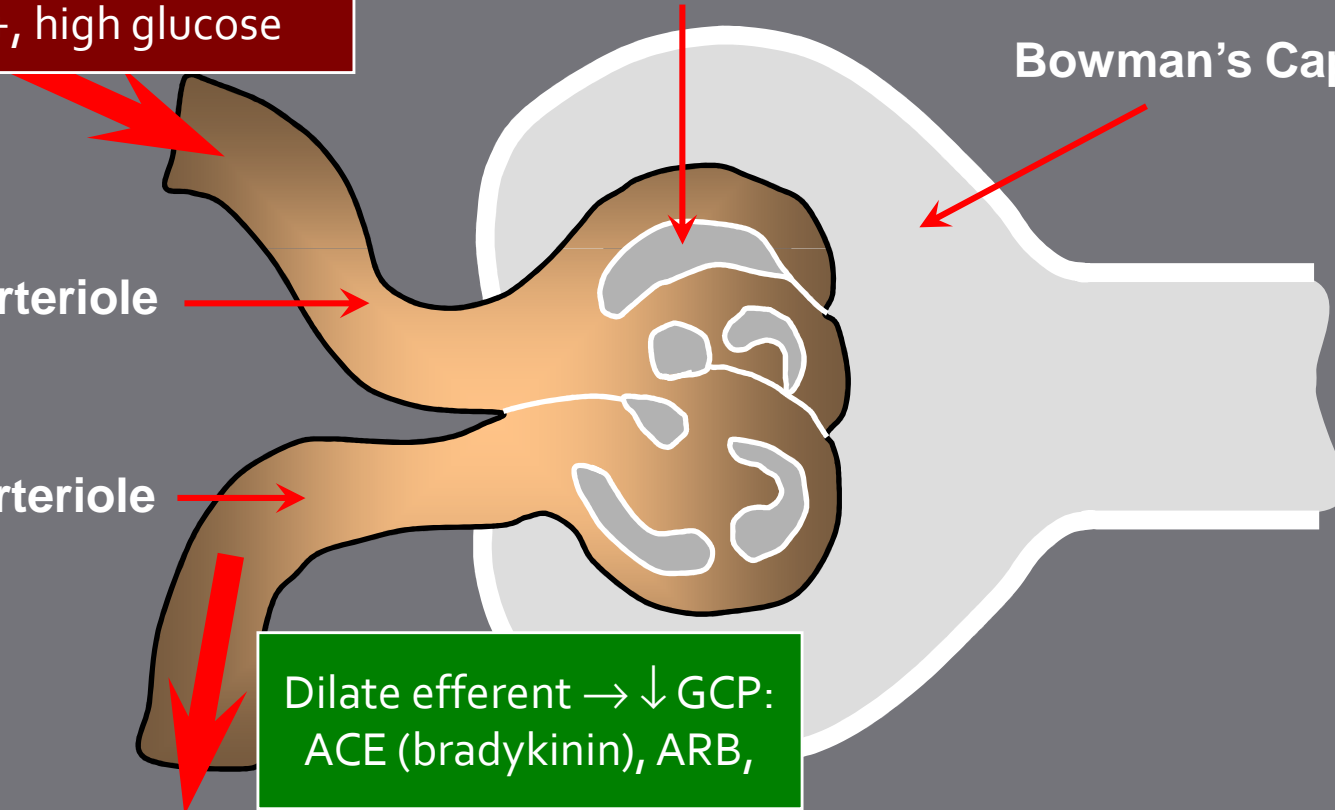
Efferent arteriole

Glomerulus

Bowman's Capsule

Dilate efferent → ↓ GCP:  
ACE (bradykinin), ARB,

↓ Glomerular pressure  
↓ Albumin Excretion Rate



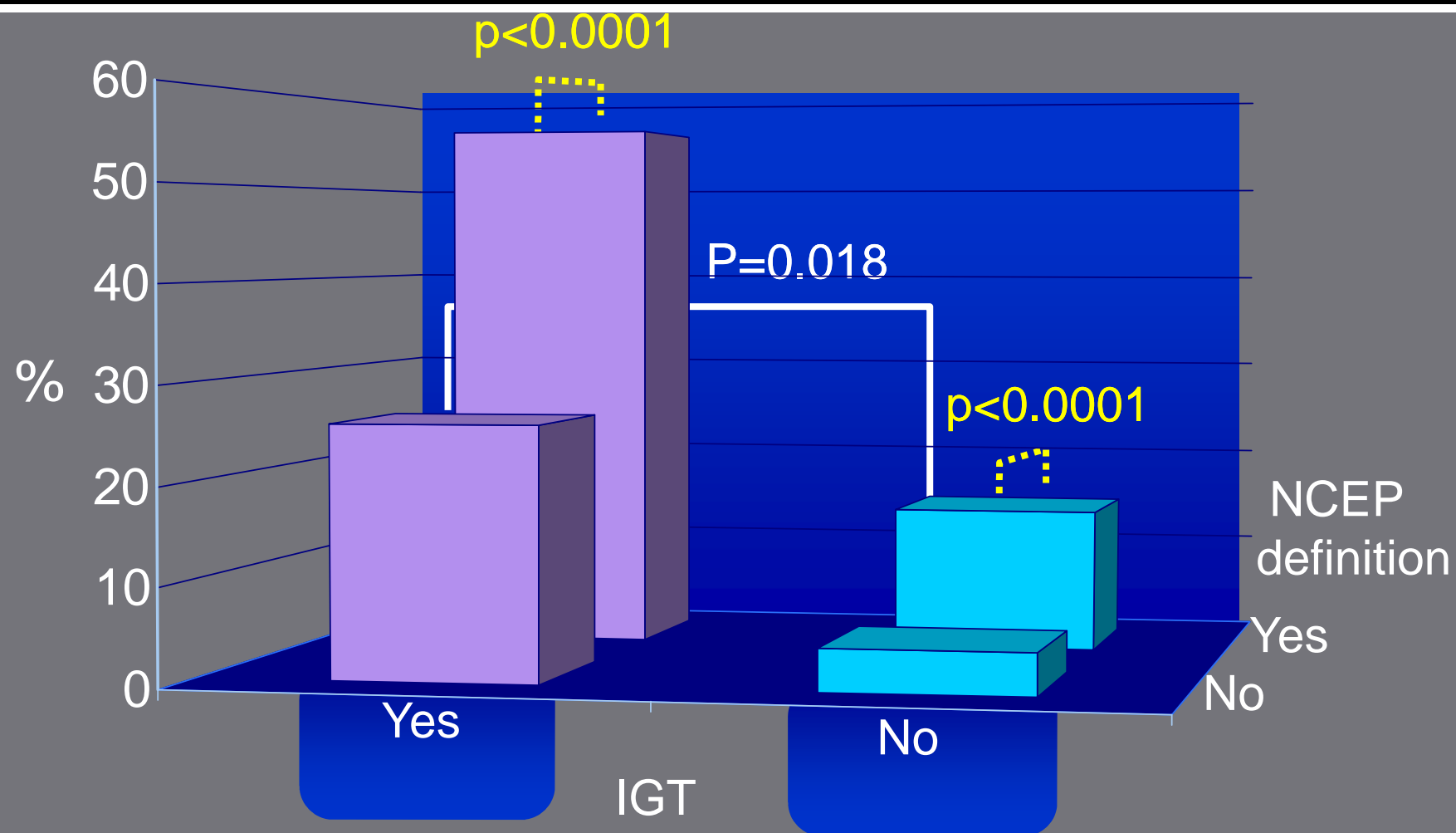


# Case Presentation #1: Elderly Hypertensive. Diabetes Prevention

You are concerned about Mrs. EJs risk of T2D and her return to previous lifestyle patterns. You counsel her that lifestyle changes have reduced the incidence of new-onset T2D in clinical trials by approximately:

1. 10%
2. 20%
3. 40%
4. 60%
5. 80%

# Incident Diabetes after Stratification by IGT and the Metabolic Syndrome

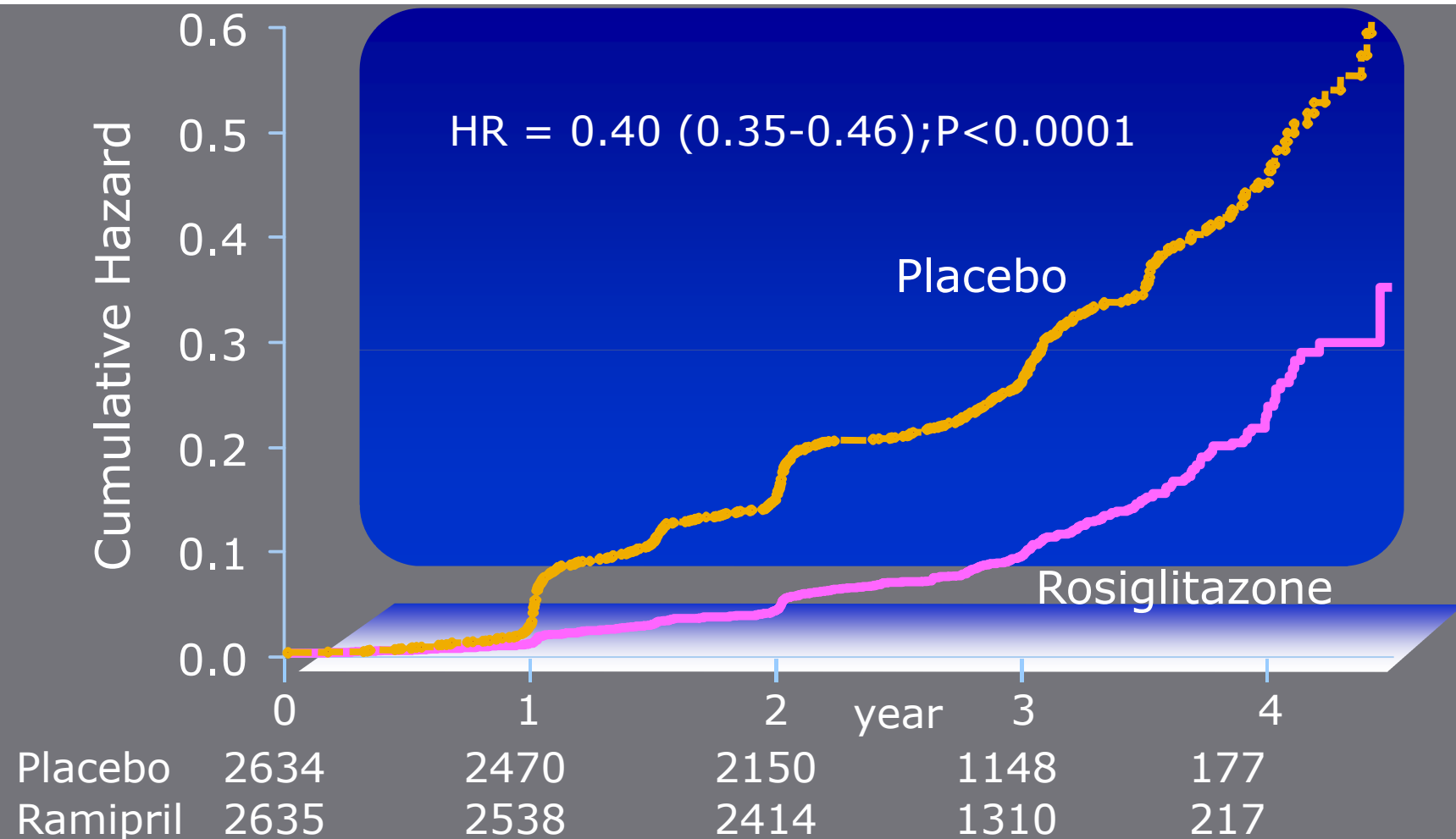


Lorenzo C et al. *Diabetes Care* 2003;26:3153-3159.

# Prevention of Type 2 Diabetes: Completed Trials in Impaired Glucose Tolerance

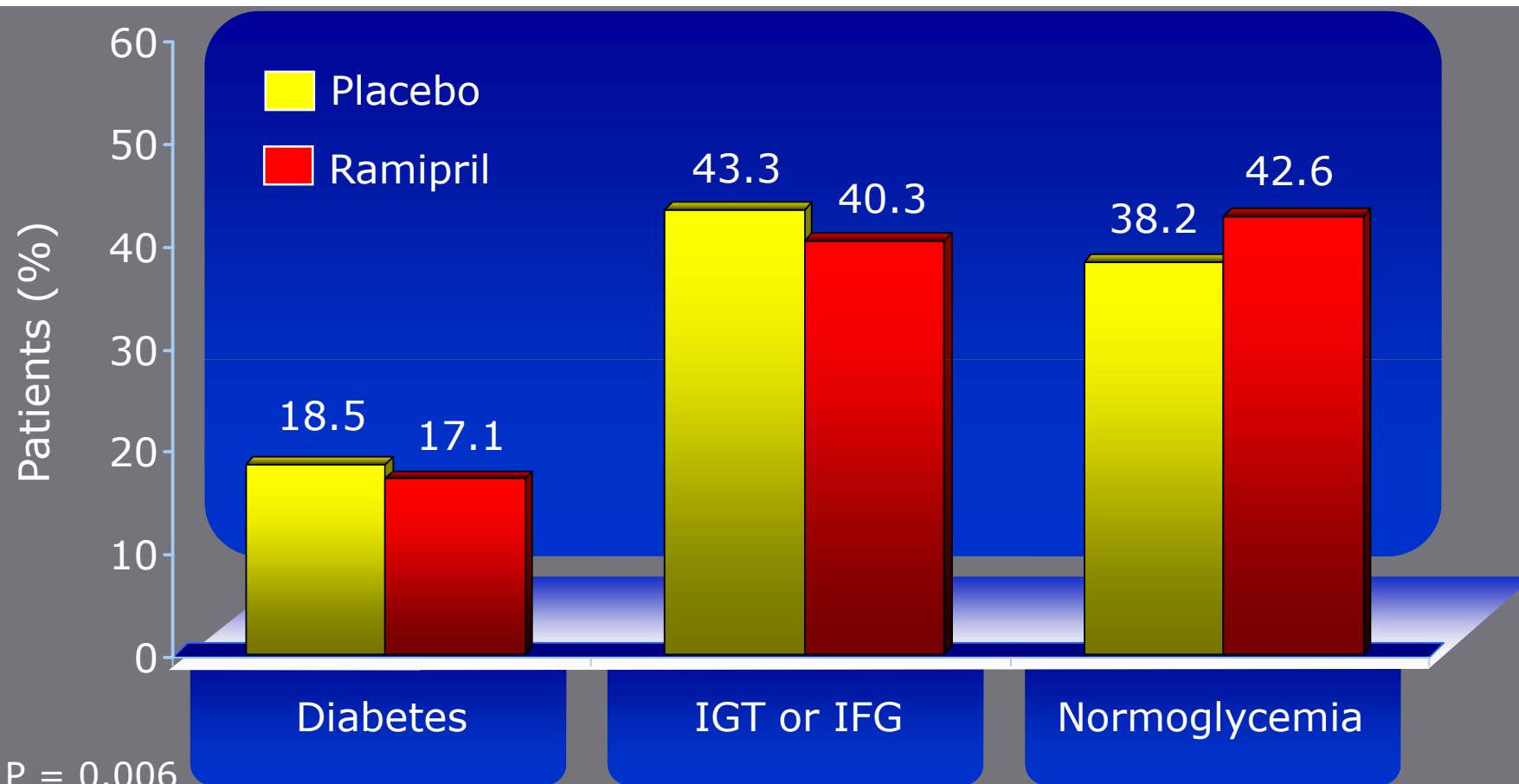
<b>Trial</b>	<b>Journal/Year</b>	<b>Description</b>	<b>Results</b>
Da Qing	Diabetes Care / 1997	Diet +/- exercise	31-46% Risk Reduction (RR)
Finnish Prevention Study (FPS)	NEJM / 2001	Intensive lifestyle	58% RR
Diabetes Prevention Program (DPP)	NEJM / 2002	Metformin	31% RR
		Lifestyle	58% RR
	Diabetes / 2005	Troglitazone	75% RR
STOP-NIDDM	Lancet / 2002	Acarbose	25% RR
TRIPOD	Diabetes / 2002	Troglitazone	55% RR
DREAM	Lancet / 2006	Rosiglitazone	62% RR
	NEJM / 2006	Ramipril	9% RR (NS)

# DREAM: Primary Outcome— Rosiglitazone



The DREAM Trial Investigators. *Lancet* 2006;368:1096-1105.

# DREAM: Ramipril Effect on Glycemic Categories



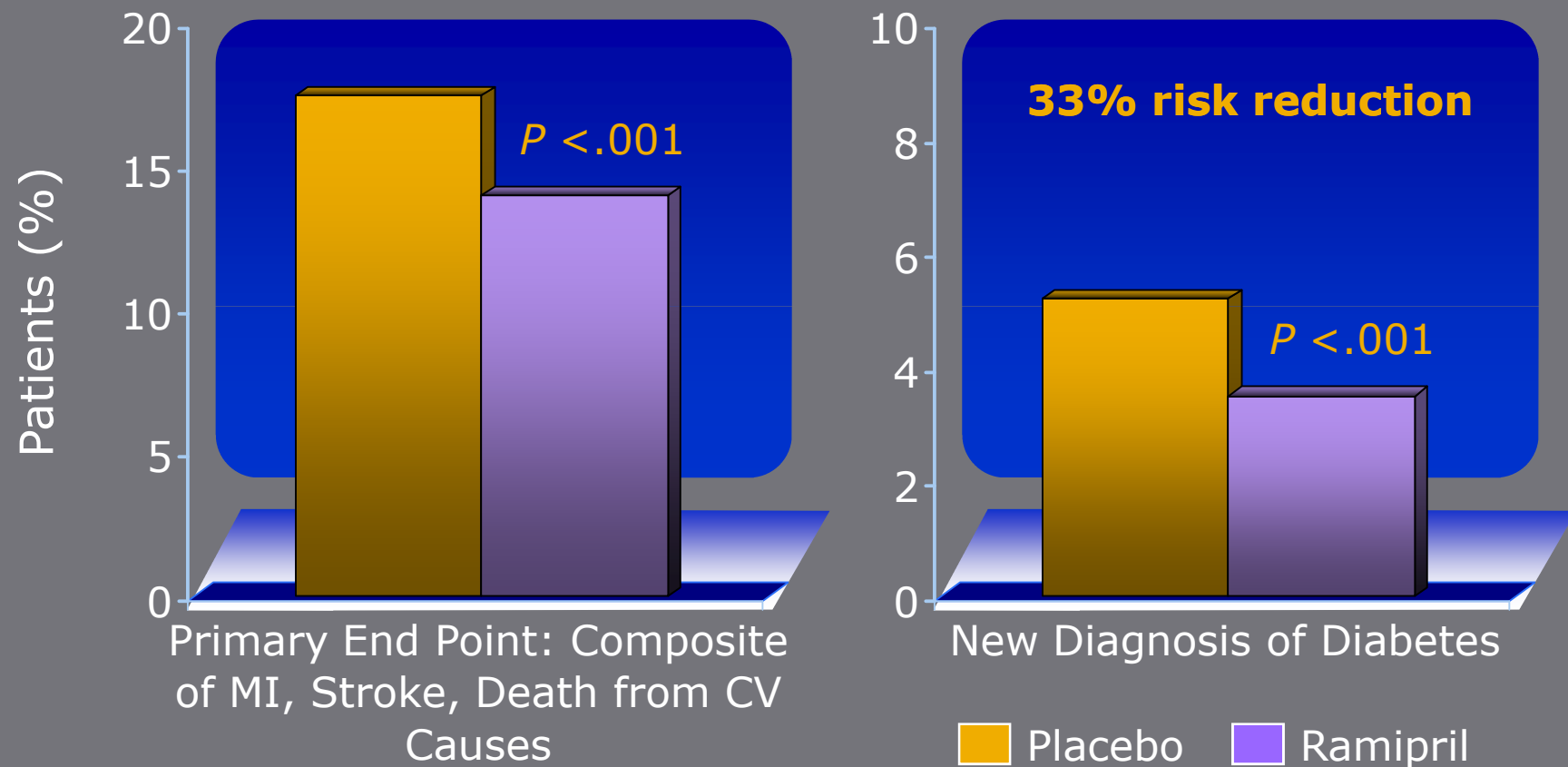
P = 0.006

IFG = impaired fasting glucose.

IGT = impaired glucose tolerance

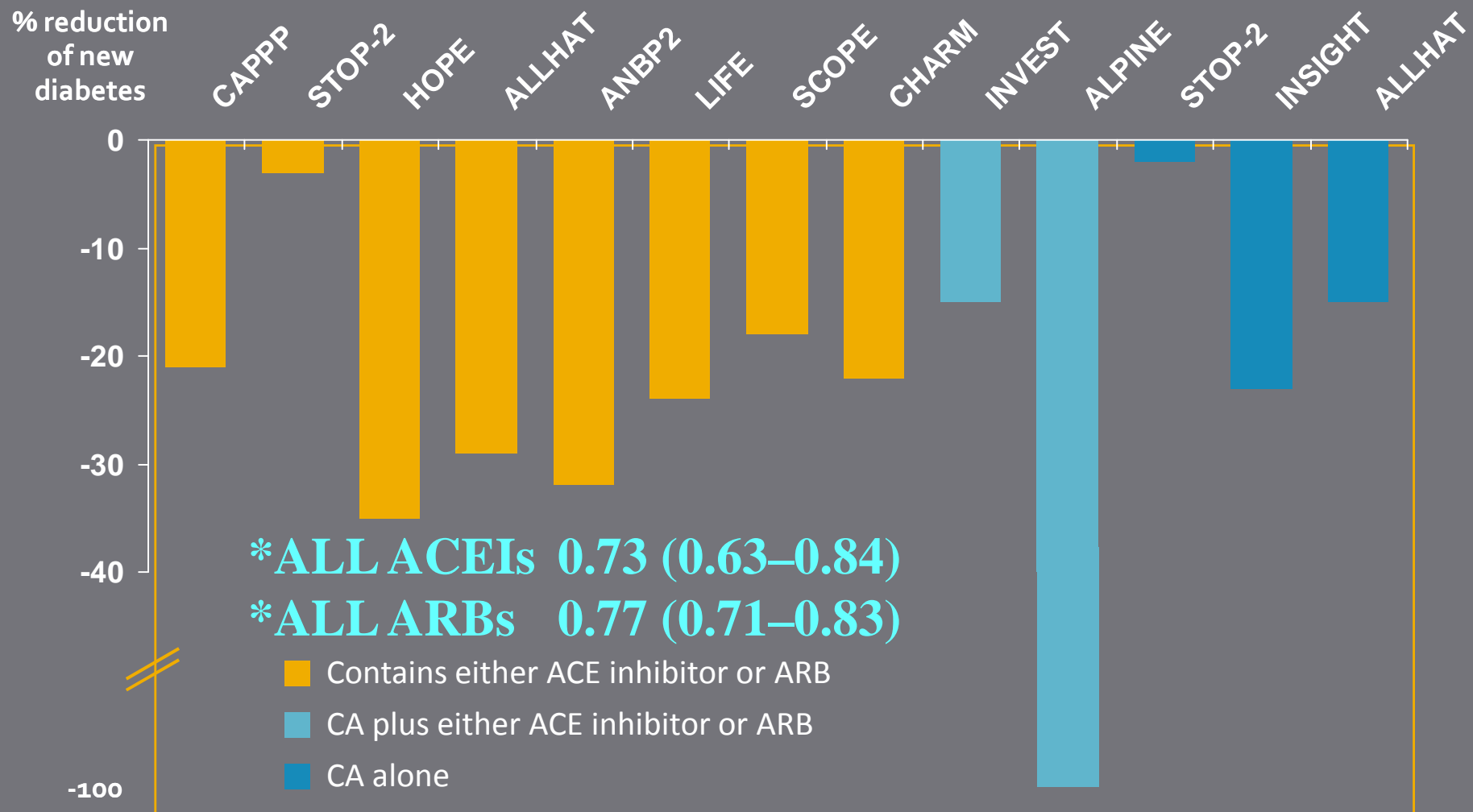
DREAM Trial Investigators. *N Engl J Med* 2006;355:1551-62.

# HOPE Study: ACE-Inhibitor Ramipril Reduces Risk of CVD and Diabetes in High-Risk Patients

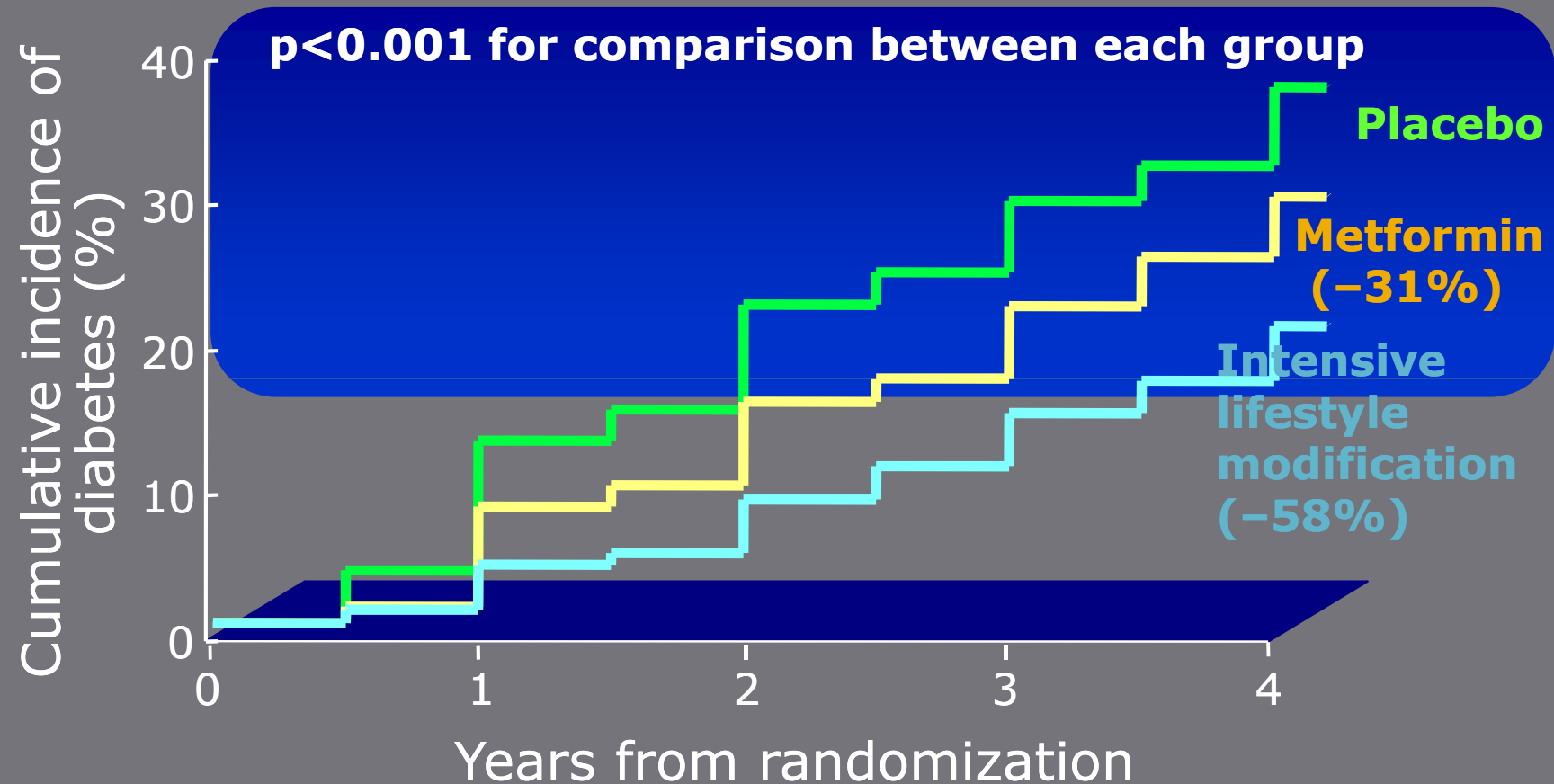


Yusuf S et al. *N Engl J Med* 2000;342:145-153.

# Cardiovascular Therapies and Risk for Development of Diabetes



# Incidence of Type 2 Diabetes: Diabetes Prevention Program (DPP)



Diabetes Prevention Program Research Group. *N Engl J Med* 2002;346:393-403.



# DASH: Beyond Blood Pressure

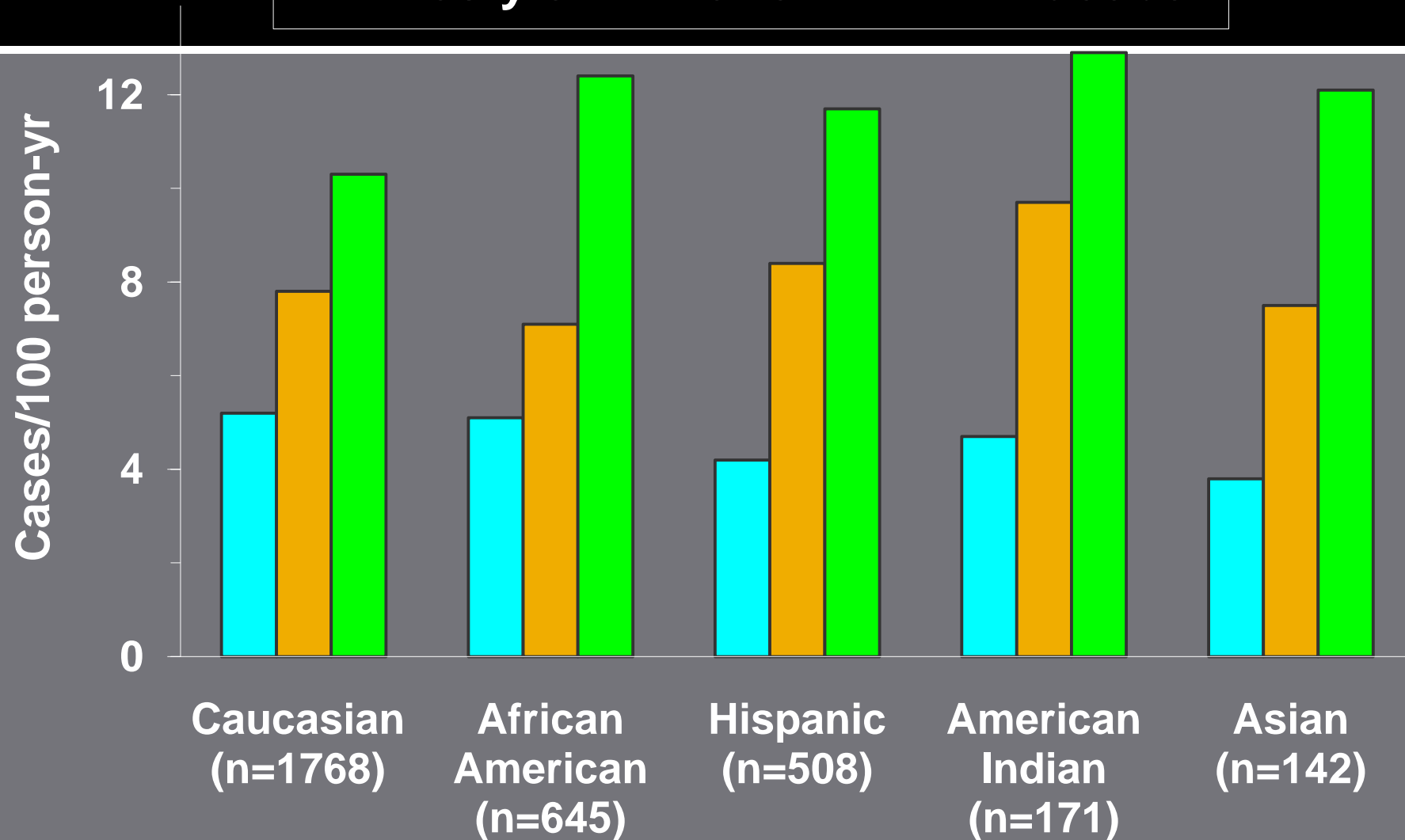
- Metabolic syndrome patients who followed a low-calorie DASH Eating Plan for 6 months lost ~30 lbs, reduced BP 12/6, TG 18, FBS 15 and waist girth 5 cm, while raising HDL 7 mg/dL in men. Changes were similar in women.
- In the Nurses' Health Study, women with diets most DASH-like diets had 24% fewer CHD events and 18% fewer strokes than women with diets least DASH-like.

Diabetes Care. 28(12):2823-31, 2005 Dec.

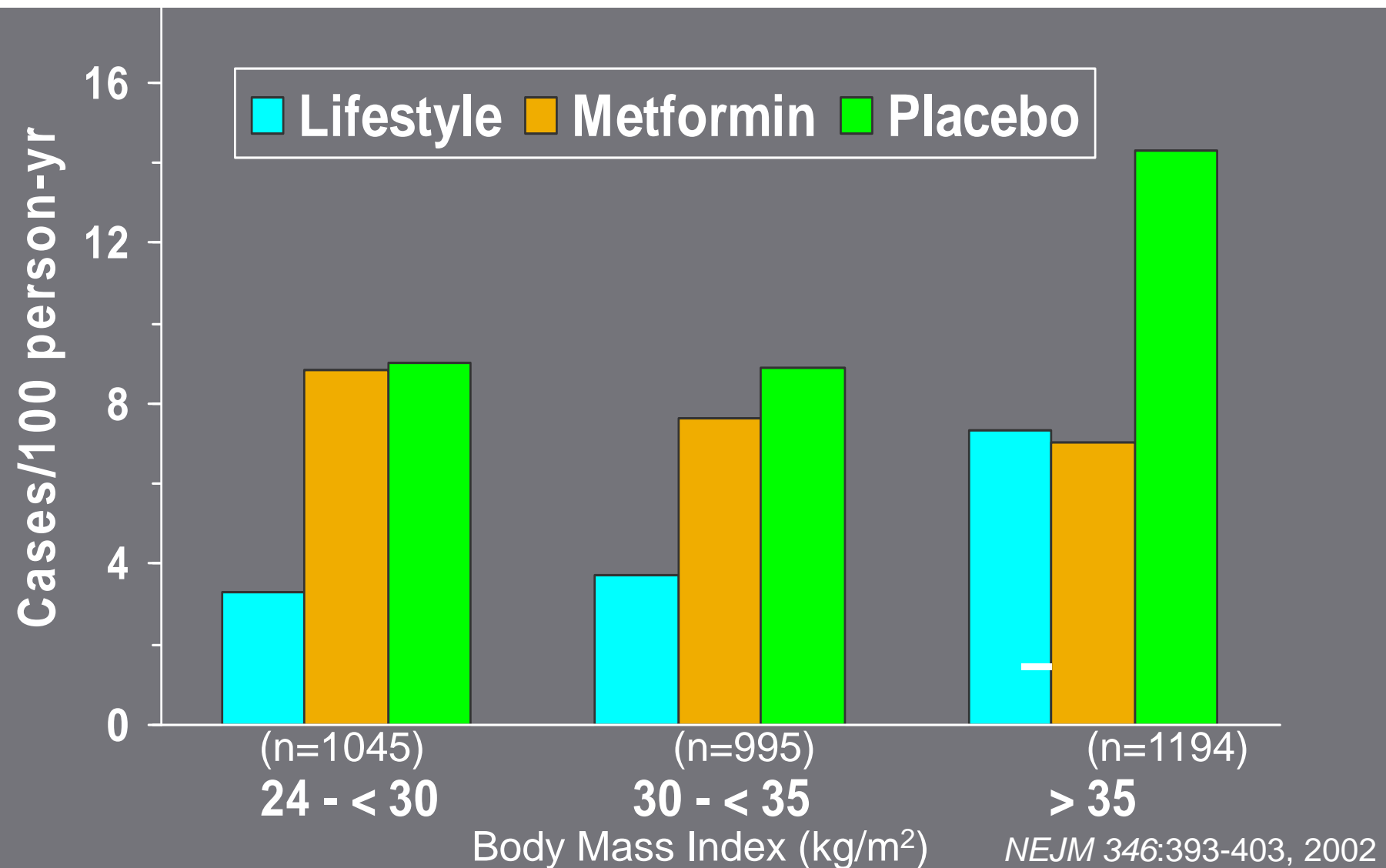
Arch Int Med. 168(7):713-20, 2008

# Diabetes Incidence Rates by Ethnicity

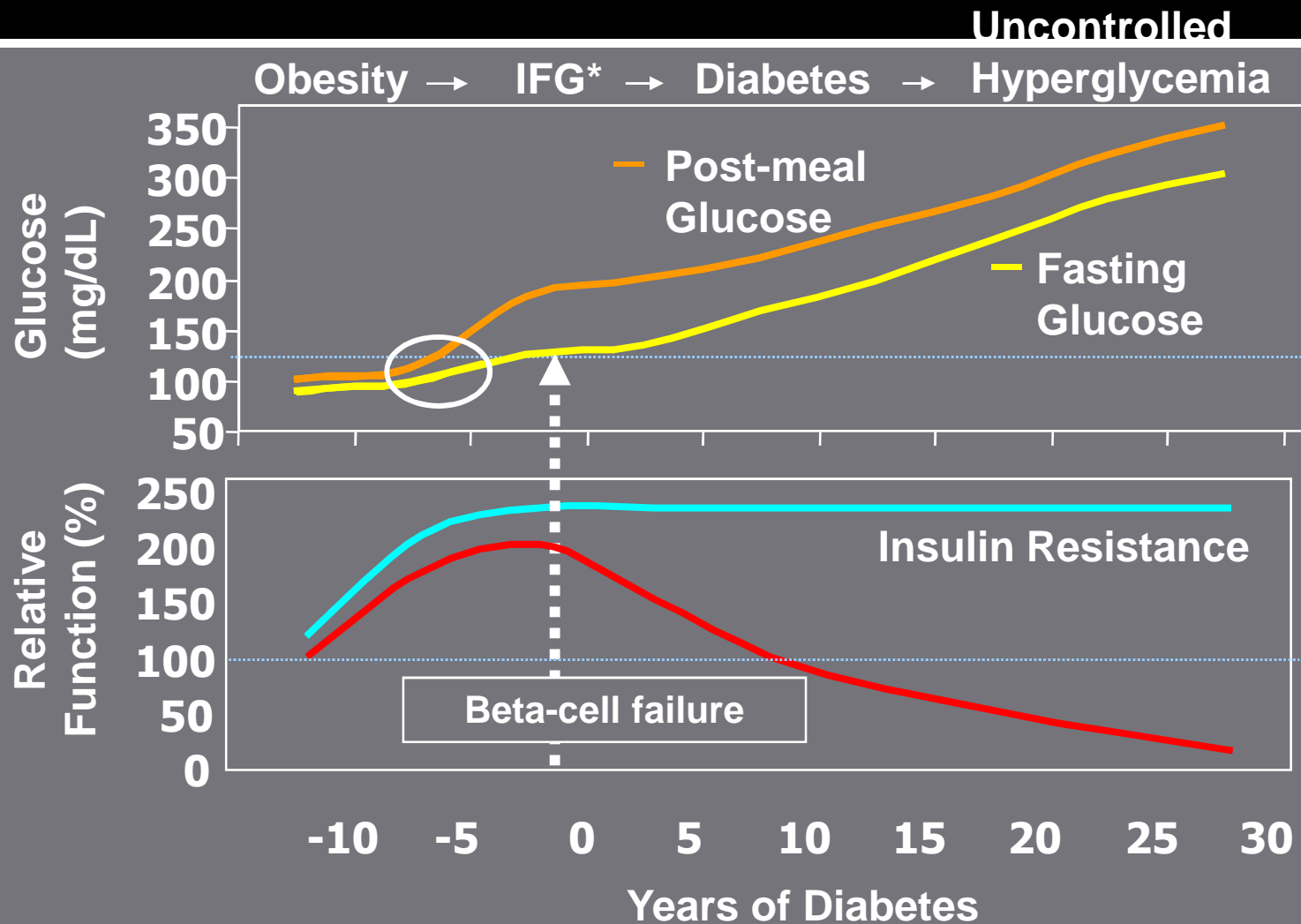
■ Lifestyle ■ Metformin ■ Placebo



# Diabetes Incidence Rates by BMI



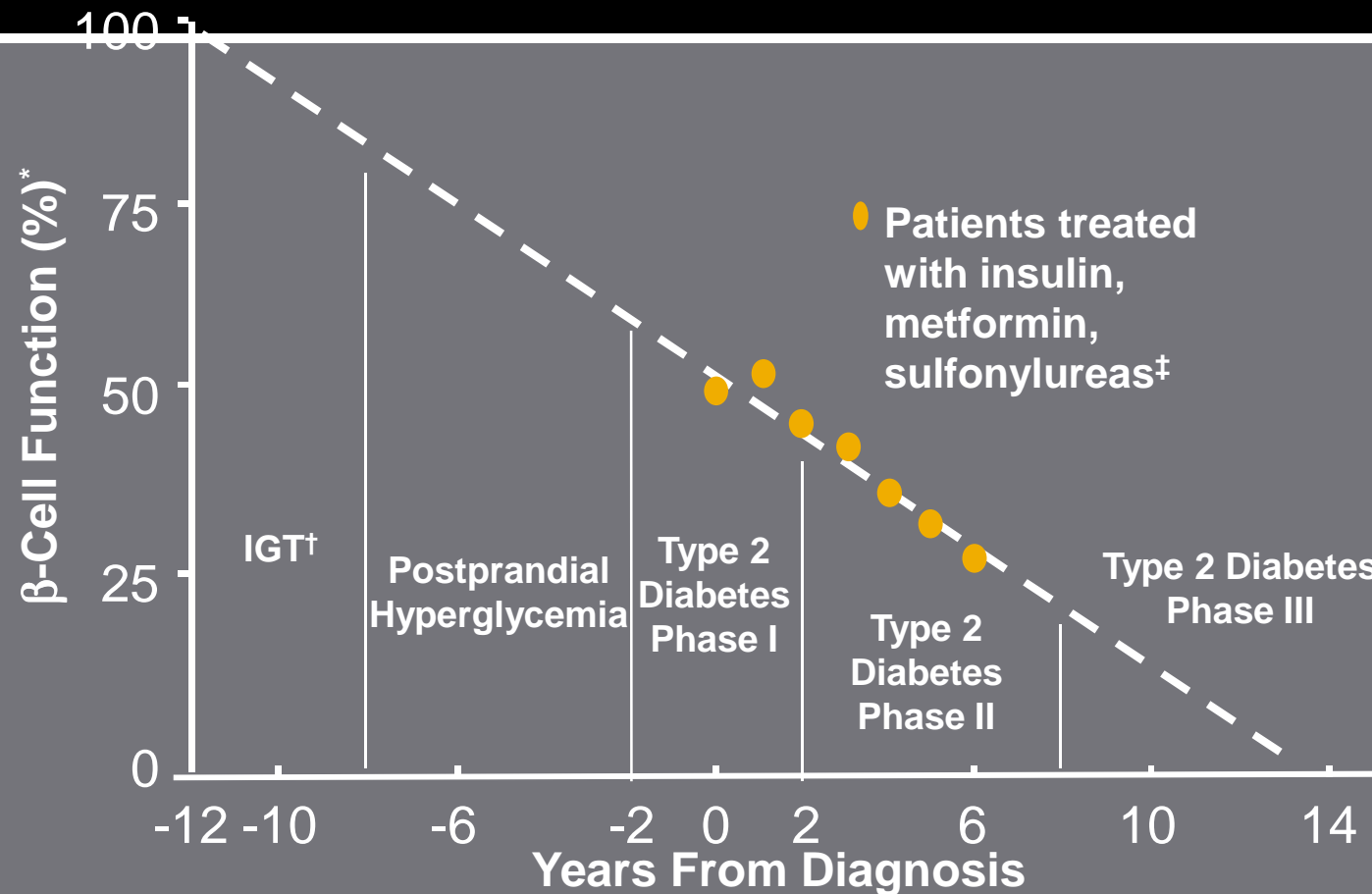
# Natural History of Type 2 Diabetes



\*IFG = impaired fasting glucose

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# UKPDS: $\beta$ -Cell Loss Over Time



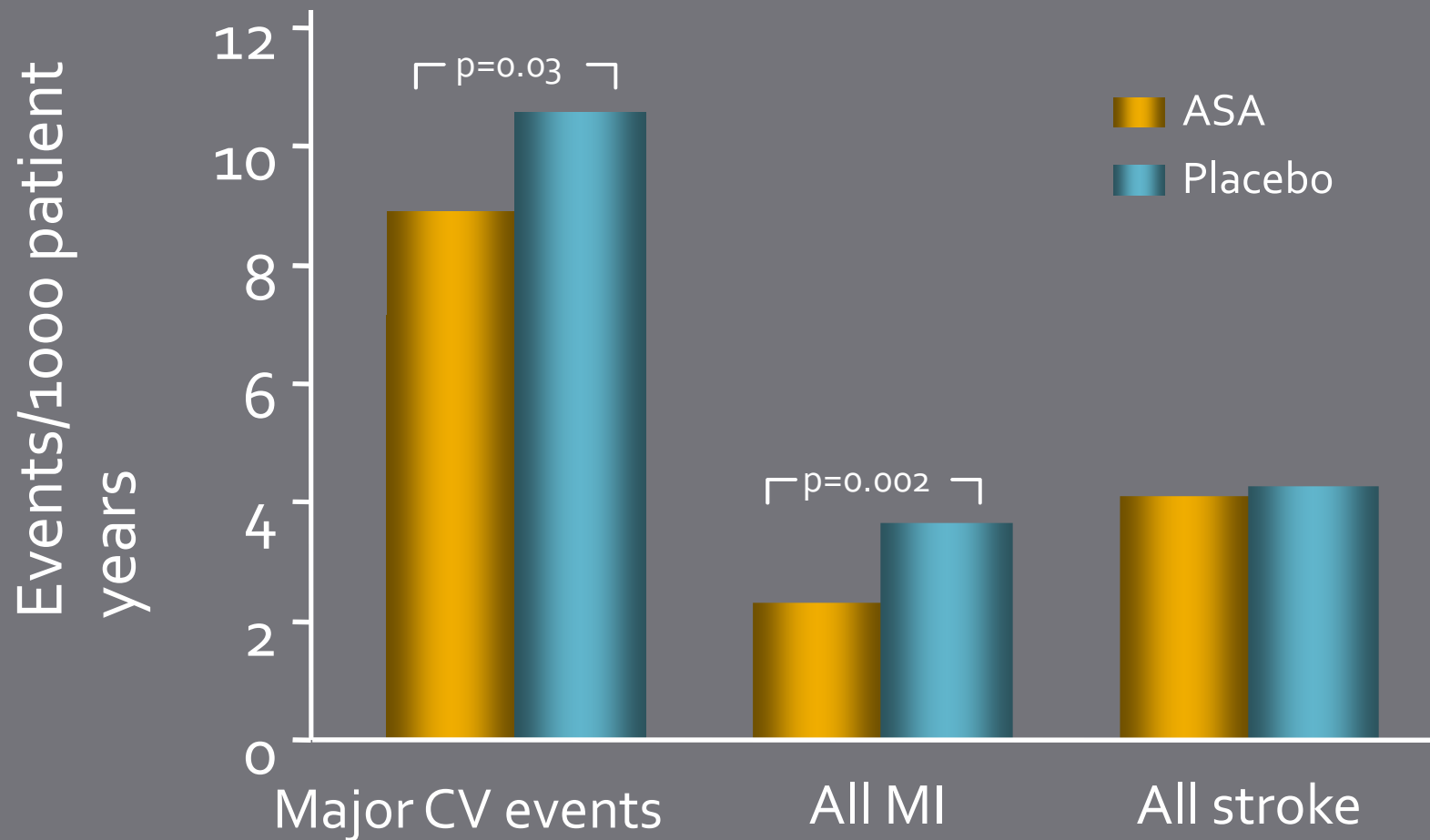
\*Dashed line shows extrapolation forward and backward from years 0 to 6 from diagnosis based on Homeostasis Model Assessment (HOMA) data from UKPDS.

<sup>†</sup>IGT=impaired glucose testing

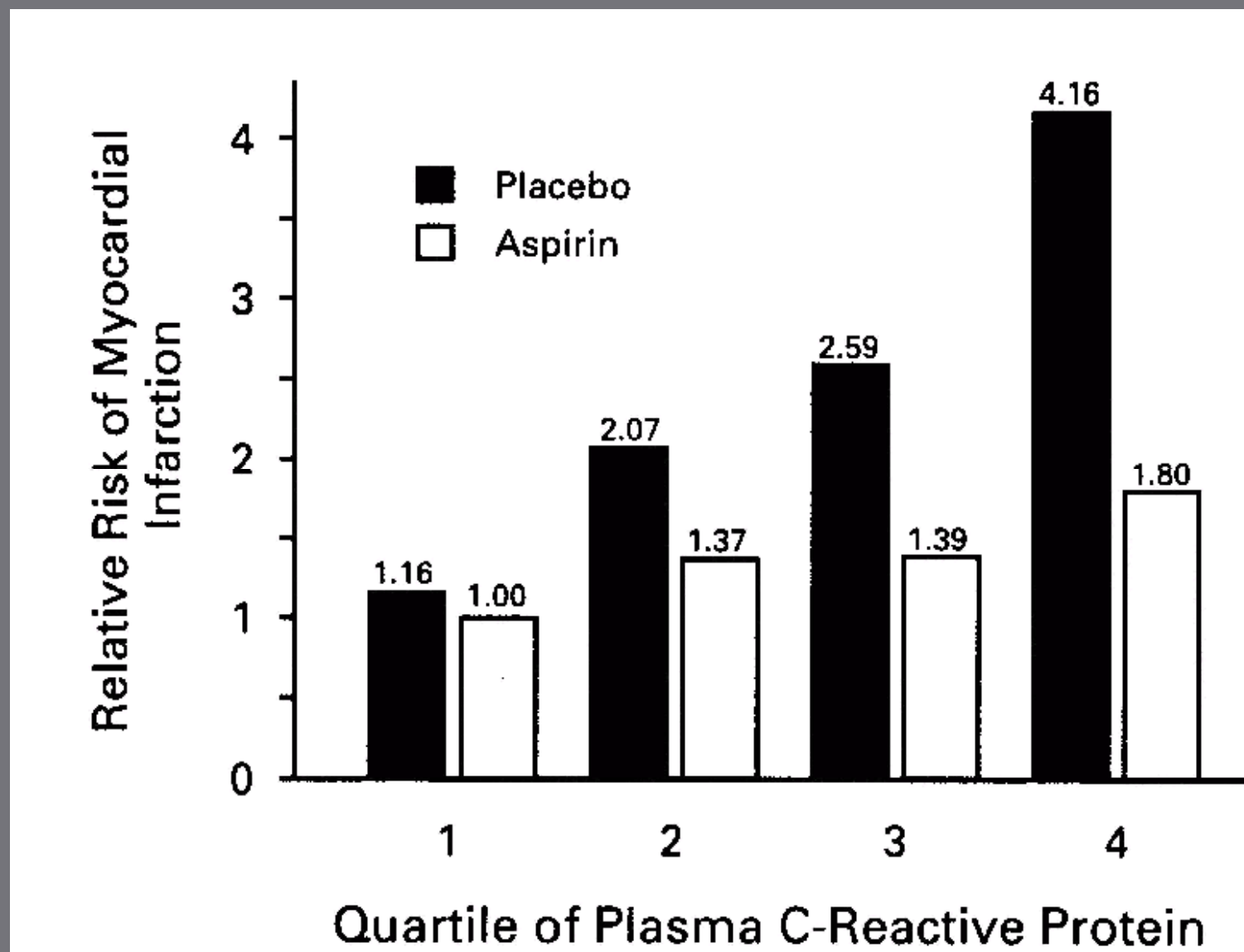
<sup>‡</sup>The data points for the time of diagnosis (0) and the subsequent 6 years are taken from a subset of the UKPDS population and were determined by the HOMA model.

Lebovitz HE. *Diabetes Rev.* 1999;7:139-153.

# ASA Reduces CV Events in Well-Treated Hypertensives: HOT Study



# Hs-CRP, Aspirin, and Risks of Future MI



Ridker PM, et. al. New Engl J of Med. 1997; 336: 973-979.

# Metabolic Syndrome: Pharmacotherapy

Blood Pressure (<140/90 for all, <130/80 for many)

- Begin with ACEI and / or ARB (for BP, DM prevention, kidney)
- CCB or low dose diuretic as 2<sup>nd</sup> agent often needed for BP
- $\beta$ -blocker if  $\uparrow$  HR, post-MI, CHF; consider ndCCB if proteinuria

Lipids (LDL <100 {optional <70}; HPS: statin for all high risk)

- With statin focus, don't forget that fibrates for MS Pts with  $\uparrow$ TG and  $\downarrow$ HDL  $\rightarrow$  ~70%  $\downarrow$  CHD (Helsinki Heart); consider fish oil

Diabetes (HbA1c <6.5%–7.0%)

- Use metformin to  $\downarrow$  glucose, minimize wt gain along with HS insulin to reduce glycemic burden

**Low dose ASA for hypercoagulable, inflammatory state**



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- Diabetes